Attachment 1

Molecular Combing

This page briefly presents the molecular combing technic, which is used to stretch macromolecules (among which DNA) in a parallel fashion, by anchoring them specifically by their extremities. More detailed informations can be found in the articles cited in the bibliography.

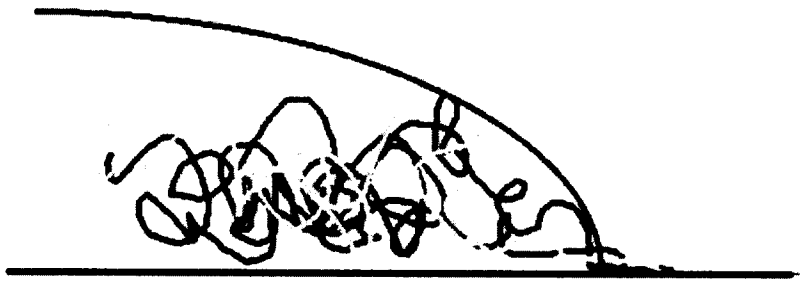
• The principle

The principle of molecular combing is analogous to that of the receding sea, which aligns algae on the beach.

In molecular combing, algae are replaced by linear macromolecules, like DNA, which can be anchored on several surfaces by their extremities only, provided the right physico-chemical conditions are used (cf [1,2]).

The front wave of the receding sea is here replaced by a meniscus, that is, the free surface of the solution in which the molecules were first dissolved.

This is explained on the following sketch:



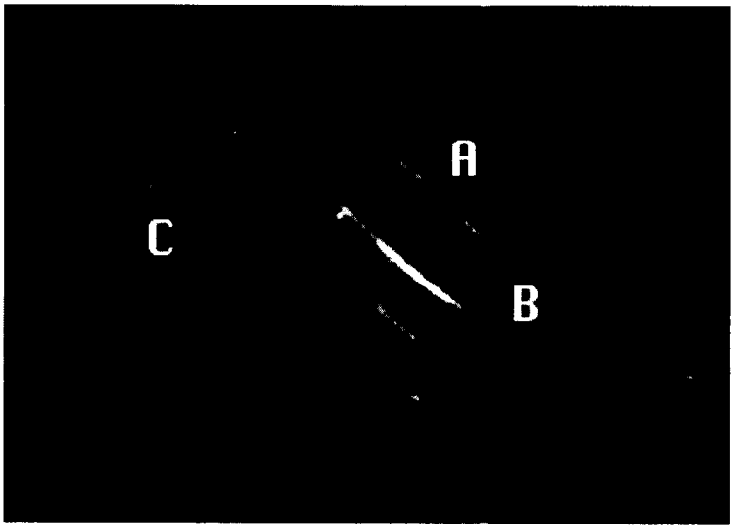
On the right is the region of the surface left by the solution, which moves leftwards. After the meniscus has receded, molecules are stretched and bound irreversibly onto the surface.

This phenomenon occurs on different kind of surfaces, and in different buffers, each case being characterized by physico-chemical parameters allowing a *specific* anchoring of the molecules by their extremities only.

• The Results

In order to visualize the results of the molecular combing of DNA, intercalating fluorescent molecules

are used (cf [3], for example). The Lambda Phage DNA, whose cristallographic length is 16.2 microns, can for instance be visualized in an epifluorescence microscope.



The preceding picture shows an example of Lambda Phage DNA molecules visualized with an ultra-sensitive camera, after combing on a surface coated with polylysine. Molecule A has a length of exactly 16.2 microns, and B is in fact made of two partially overlapping molecules. Molecule C is anchored by its two extremities, which yields a loop shape (cf [2]).

Two videos on molecular combing.

• Some Applications

Among the many possible uses of molecular combing, we focus here on those we are actually working on in our laboratory, or in collaboration with other groups:

- Gene Physical Mapping

  This activity aims at locating nucleotidic sequences on combed DNA. The sequences hybridize on the corresponding target sequences on the combed DNA, and are furtheron detected using fluorescent antibodies (cf page: fluorescent hybridization or *FISH*). Their relative position can be determined very precisely, since the stretching of combed DNA is homogeneous all over the surface.

- Genetic Diagnostic

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- in situ PCR

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Bibliography & References

Alignment and Sensitive Detection of DNA by a Moving Interface.
A. Bensimon, A. Simon, A. Chiffaudel, V. Croquette, F. Heslot and D. Bensimon.
[1] **Science**, 265, pp 2096-2098 (1994).
abstract

Stretching DNA with a receding meniscus: Experiments and Models.
D. Bensimon, A. J. Simon, V. Croquette and A. Bensimon.
[2] **Phys. Rev. Lett.**, 76, pp 4754-4757 (1995).
abstract

[3] TOTO: an example of a fluorescent intercalating molecule

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